

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamxgl614

PASSWORD:

LOGINID/PASSWORD REJECTED

The loginid and/or password sent to STN were invalid.
You either typed them incorrectly, or line noise may
have corrupted them.

Do you wish to retry the logon?

Enter choice (y/N):

Connecting via Winsock to STN

LOGINID:

SSPTAMXG1614

STNLOGON timed out

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAMXG1614

PASSWORD:

LOGINID/PASSWORD REJECTED

The loginid and/or password sent to STN were invalid.
You either typed them incorrectly, or line noise may
have corrupted them.

Do you wish to retry the logon?

Enter choice (y/N):

Connecting via Winsock to STN

LOGINID:

ssptamxgl614

STNLOGON timed out

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamxgl614

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 JUL 20 Powerful new interactive analysis and visualization software,
STN AnaVist, now available
NEWS 4 AUG 11 STN AnaVist workshops to be held in North America
NEWS 5 AUG 30 CA/CAPLUS - Increased access to 19th century research documents
NEWS 6 AUG 30 CASREACT - Enhanced with displayable reaction conditions
NEWS 7 SEP 09 ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 8 OCT 03 MATHDI removed from STN
NEWS 9 OCT 04 CA/CAPLUS-Canadian Intellectual Property Office (CIPO) added
to core patent offices
NEWS 10 OCT 06 STN AnaVist workshops to be held in North America

NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 20:09:42 ON 06 OCT 2005

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 20:10:29 ON 06 OCT 2005

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 6 Oct 2005 VOL 143 ISS 15

FILE LAST UPDATED: 5 Oct 2005 (20051005/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s 109577-83-5/rn
      6 109577-83-5
      0 109577-83-5D
L1      6 109577-83-5/RN
      (109577-83-5 (NOTL) 109577-83-5D )
```

```
=> s ll and (respiratory or pulmonary)
      111919 RESPIRATORY
      74572 PULMONARY
L2      2 L1 AND (RESPIRATORY OR PULMONARY)
```

```
=> d 1-2 bib abs
```

```
L2  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
AN  2002:320348  CAPLUS
DN  137:272760
TI  Intracellular localization of 7-benzylamino-6-chloro-2-piperazino-4-
    pyrrolidino-pteridine in membrane structures impeding the inhibition of
    cytosolic cyclic AMP-specific phosphodiesterase
AU  Marko, Doris; Merz, Karl-Heinz; Kunz, Claudia; Muller, Anja; Tarasova,
    Nadya; Eisenbrand, Gerhard
CS  Division of Food Chemistry and Environmental Toxicology, Department of
    Chemistry, University of Kaiserslautern, Kaiserslautern, D-67663, Germany
SO  Biochemical Pharmacology (2002), 63(4), 669-676
    CODEN: BCPCA6; ISSN: 0006-2952
PB  Elsevier Science Inc.
DT  Journal
LA  English
AB  7-Benzylamino-6-chloro-2-piperazino-4-pyrrolidino-pteridine (DC-TA-46) is
    a potent inhibitor of the rolipram-sensitive cAMP-specific
    phosphodiesterase isoenzyme family PDE4. DC-TA-46 inhibits
    cAMP-hydrolysis of PDE4 isolated from solid tumors of the human large cell
    lung tumor xenograft LXFL529 in the nanomolar range (IC50=16±5 nM).
    Tumor cells, however, are growth inhibited only in the lower micromolar
    range as shown for the human large cell lung carcinoma cell line LXFL529L.
    To investigate reasons for the discrepancy between IC50 values for target
    inhibition and inhibition of cell growth, uptake, subcellular distribution
    and elimination of the compound were measured. DC-TA-46 was rapidly taken
    up by the cells, predominantly localized in intracellular membranes.
    Elimination was slow, with 70% of the compound still persisting in the
    membranes 50 h after withdrawal. Confocal laser scanning microscopy
    showed a clear colocalization with a fluorescent marker for the
    endoplasmatic reticulum (ER). As a result of the subcellular
    localization, the membrane-bound PDE activity of LXFL529L cells was
    effectively inhibited by DC-TA-46 (IC50=0.06±0.02 µM). In contrast,
    inhibition of the cytosolic PDE activity was only achieved at concns. >1
    µM (IC50=2.0±0.5 µM), in the concentration range where also growth
    inhibition was observed. Thus, the inhibition of the intracellular PDE
    activity in the different cellular compartments appears to represent an
    important parameter for the evaluation of the inhibitory properties at
    least of this class of compds.
RE.CNT 15  THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
      ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
L2  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
AN  2002:320347  CAPLUS
DN  137:272904
TI  7-Benzylamino-6-chloro-2-piperazino-4-pyrrolidino-pteridine, a potent
    inhibitor of cAMP-specific phosphodiesterase, enhancing nuclear protein
    binding to the CRE consensus sequence in human tumour cells
```

AU Wagner, Barbara; Jakobs, Sandra; Habermeyer, Michael; Hippe, Frankie;
Cho-Chung, Yoon Sang; Eisenbrand, Gerhard; Marko, Doris
CS Division of Food Chemistry and Environmental Toxicology, Department of
Chemistry, University of Kaiserslautern, Kaiserslautern, D-67663, Germany
SO Biochemical Pharmacology (2002), 63(4), 659-668
CODEN: BCPA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal
LA English

AB The cAMP-specific phosphodiesterase isoenzyme family PDE4 represents the highest cAMP-hydrolyzing activity in many human cancer cell lines including the human large cell lung carcinoma cell line LXFL529L. Treatment of LXFL529L cells with the potent PDE4 inhibitor 7-benzylamino-6-chloro-2-piperazino-4-pyrrolidino-pteridine (DC-TA-46) induces dose-dependent growth inhibition. Cells are arrested in the G1-phase of the cell cycle and the induction of apoptosis is observed. In this study, the authors investigated the effect of DC-TA-46 on downstream elements of the cAMP-pathway. DC-TA-46 mediated inhibition of PDE4 activity in LXFL529L cells resulted in an increase of the intracellular cAMP level and significant induction of the activity of protein kinase A (PKA). The regulatory PKA subunit RI α was predominantly expressed in LXFL529L cells. In contrast to effects induced by cAMP analogs like 8-Cl-cAMP, the expression of the regulatory subunits of PKA remained unaffected by DC-TA-46. Treatment of LXFL529L cells with DC-TA-46 enhanced the binding of nuclear proteins to the cAMP-responsive element (CRE) consensus sequence TGACGTCA in a time- and dose-dependent manner, indicating the activation of transcription factors by PKA phosphorylation.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 219128-24-2/rn
1 219128-24-2
0 219128-24-2D
L3 1 219128-24-2/RN
(219128-24-2 (NOTL) 219128-24-2D)

=> d bib abs

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:703904 CAPLUS
DN 130:90061
TI Synthesis of 7-Benzylamino-6-chloro-2-piperazino-4-pyrrolidinopteridine and Novel Derivatives Free of Positional Isomers. Potent Inhibitors of cAMP-Specific Phosphodiesterase and of Malignant Tumor Cell Growth
AU Merz, Karl-Heinz; Marko, Doris; Regiert, Thomas; Reiss, Guido; Frank, Walter; Eisenbrand, Gerhard
CS Departments of Chemistry Division of Food Chemistry and Environmental Toxicology and Division of Inorganic Chemistry, University of Kaiserslautern, Kaiserslautern, D-67663, Germany
SO Journal of Medicinal Chemistry (1998), 41(24), 4733-4743
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB 7-Benzylamino-6-chloro-2-piperazino-4-pyrrolidinopteridine (I) is a potent inhibitor of the cAMP-specific phosphodiesterase isoenzyme family PDE4 and induces growth inhibition in a panel of tumor cell lines. In this study, we describe a synthesis that yields I and novel derivs. free of positional isomers. The synthesis of alkylamino substituted pteridines is based on the successive nucleophilic aromatic substitution of the chlorine atoms of 2,4,6,7-tetrachloropteridine. For the reaction with secondary amines, the positional order of reactivity was found to be C4 > C7 > C2 > C6. Final structural proof is given by X-ray crystallog. To unravel structural elements of I crucial for the interaction with the target enzyme, the

compound was modified systematically. The impact of the modifications on activity was tested by evaluating the ability of the compds. to inhibit cAMP hydrolysis by cAMP-specific phosphodiesterase (PDE4) purified from the solid human large cell lung tumor xenograft LXFL529. Growth inhibitory properties were determined by in vitro treatment of the resp. cell line LXFL529L using the sulforhodamine B assay (SRB). The results show that for high activity, the heterocyclic substituent in position 2 of the pteridine ring system requires the presence of a basic nitrogen in 4'-position, as represented by piperazine.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN.U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	21.09	21.30
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-2.19	-2.19

STN INTERNATIONAL LOGOFF AT 20:12:50 ON 06 OCT 2005